

ABSTRACT

The present invention provides novel purified and isolated nucleic acid sequences encoding procoagulant-active FVIII proteins. The nucleic acid sequences of the present invention encode amino acid sequences corresponding to known human FVIII sequences, wherein residue Phe309 is mutated. The nucleic acid sequences of the present invention also encode amino acid sequences corresponding to known human FVIII sequences, wherein the APC cleavage sites, Arg336 and Ile562, are mutated. The nucleic acid sequences of the present invention further encode amino acid sequences corresponding to known human FVIII sequences, wherein the B-domain is deleted, the von Willebrand factor binding site is deleted, a thrombin cleavage site is mutated and an amino acid sequence spacer is inserted between the A2- and A3-domains. Methods of producing the FVIII proteins of the invention, nucleotide sequences encoding such proteins, pharmaceutical compositions containing the nucleotide sequences or proteins, as well as methods of treating patients suffering from hemophilia, are also provided.